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REMARKS

Claims 32-36, 38-41, 52 and 53 are pending. Claims 1-31, 37, and 42-51 stand cancelled. Applicants have amended claims 32 and 52 to more clearly delineate the instant invention. Support for the amendment to claim 32 can be found at least at page 30, line 17 to page 31, line 10. Support for the amendment to claim 52 can be found at least at page 65, lines 17-19 and page 28, lines 2-7 and page 30, lines 13-16. No new matter is introduced by the presented amendments.

Rejection under 35 U.S.C. § 103(a)

Claims 32-36, 38-41, 52, and 53 are rejected as obvious over Sakanaka et al. (Jpn. J. Pharmacol. 67, Suppl. I, 297P, 1995), in view of Liu et al. (US Patent 4,708,949), and in view of Zhang et al. (Acta Pharmacologica Sinica 17(1), 44-48, 1996). It is asserted in the Action that: (1) Sakanaka teaches the use of ginseng saponins and ginsenoside Rb1 to prevent ischemia-induced learning disability and rescued ischemic hippocampus CA1 neuron in gerbils; (2) Liu teaches methods of treating a patient suffering from cerebrovascular disease and impaired neurofunction with a pharmaceutical composition comprising ginsenoside; and (3) Zhang teaches that ginsenoside Rb1 protected rat brains from cerebral infarction, wherein the concentration in a rat model was 10 mg/kg to 40 mg/kg. It is then alleged that the combination of (1), (2), and (3) renders the Applicants' instantly claimed subject matter obvious.

Applicants disagree but have amended claim 32 to include a dose or dosages of ginsenoside Rb_1 or its salts that are adjusted to between 0.000167 mg/kg/day and 1.67 mg/kg/day. Support for the amendment can be found at least at page 30, line 17 to page 31, line 10. The amount of ginsenoside Rb_1 to be administered to a patient weighing 60 kg is described, with the lower limit of the daily doses being 0.1 mg or more or 1/10 thereof, and the upper limit of the dose is preferably 0.1 g or less per day. The lower limit of 0.000167 mg/kg/day is thus calculated from 1/10 of 0.1 mg administered to a patient of 60 kg, per day. The upper limit of 1.67 mg/kg/day is calculated from

0.1 g administered to a patient of 60 kg per day.

As an initial matter, Applicants wish to point out that the Sakanaka reference is an abstract of a presentation, and the full contents of the presentation were disclosed in Wen, T-C. et al. Acta Neuropathol (1996), 91, p. 15-22. A copy of the Wen reference was provided with the response submitted on April 10, 2006.

The Sakanaka and Wen references are directed towards the administration of ginsenoside Rb_1 at a dose of 10 mg/kg/day or 20 mg/kg/day to prevent transient forebrain ischemia. No positive effects were observed when treating animals with transient forebrain ischemia, indicating no therapeutic effect. Additionally, Sakanaka and Wen describe that the dosage of 10 mg/kg/day is less effective than the dosage of 20 mg/kg/day in the prevention of nerve cell death induced by transient forebrain ischemia.

Neither the Sakanaka reference nor the Wen reference teach or suggest a method of treating a traumatic or compression injury of a nervous tissue, and therefore are distinct from the instant invention. Additionally, the Sakanaka and Wen references clearly demonstrate that, for the prevention of transient forebrain ischemia, smaller dosages are less effective. Therefore, Applicants submit that claim 32 as amended provides for the unexpected result wherein a patient suffering from a traumatic or compression injury of a nervous tissue is treated with a lower dosage of ginsenoside Rb_1, relative to the dosage of Sakanaka required to prevent transient forebrain ischemia. Therefore, Sakanaka does not provide a motivation or reasonable expectation of success to arrive at the method described in Applicant's amended claim 32.

It is also alleged that the Liu reference teaches a method of treating cerebral vascular disease using a pharmaceutical composition comprising ginsenoside. As the reference is understood, a four-component composition is administered to treat a cerebral vascular disease, wherein the ginsenoside extract is one component. Applicants submit that there is no teaching or

suggestion of administration of a dosage of ginsenoside Rb_1 of 0.000167 mg/kg/day to 1.67 mg/kg/day, as is recited in the Applicants' amended claim 32. Additionally, there is no teaching or suggestion that the composition using ginsenoside Rb_1 is effective to treat cerebral vascular disease, wherein the ginsenoside Rb_1 is the pharmaceutically active species. Therefore, any combination of the Sakanaka reference with Liu does not provide a motivation or reasonable expectation of success to arrive at the method described in Applicant's amended claim 32. Additionally, any combination of Sakanaka and Liu does not provide all of the claim limitations of Applicants' claim 32, as Liu does not provide for a dosage range of ginsenoside Rb_1 of 0.000167 mg/kg/day to 1.67 mg/kg/day. Reconsideration and withdrawal of the rejection is respectfully requested.

It is further alleged that Zhang teaches concentrations of ginsenoside Rb_1 of 10 mg/kg to 40 mg/kg, when used in rats to prevent focal brain ischemia. Regarding the treatment of cerebral infarction, Zhang shows preventative effects but no therapeutic effects at a dose of 40 mg/kg of ginsenoside Rb_1. Additionally, Zhang teaches that a dose of 10 mg/kg is far less effective than the dose of 40 mg/kg. Therefore, Applicants submit that the instant claim 32 as amended provides for the unexpected result wherein a patient suffering from a traumatic or compression injury of a nervous tissue is treated with a lower in dosage of ginsenoside Rb_1, relative to the dosage required to prevent focal brain ischemia (as in Zhang).

Therefore, Sakanaka in combination with Liu and Zhang, does not provide a motivation or reasonable expectation of success to arrive at the method described in Applicant's amended claim 32. Additionally, Sakanaka in combination with Liu and Zhang, does not provide all of the claim limitations of Applicants' claim 32, as Zhang does not provide for a dosage range of ginsenoside Rb_1 of 0.000167 mg/kg/day to 1.67 mg/kg/day.

For at least the foregoing reasons, the §103 rejection should be withdrawn. To establish a *prima facie* case of obviousness, three basic criteria must be met: (1) there must be some suggestion

or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference(s) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). See MPEP § 2143.

In the present case, there is no suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify or combine the cited references to arrive at the presently-claimed invention, nor is there any reasonable expectation of success. A *prima facie* case of obviousness therefore cannot be established, and the rejection must be withdrawn.

In view of the above amendments remarks, Applicants believe the pending application is in condition for allowance. Should any of the claims not be found to be allowable, the Examiner is requested to telephone Applicants' undersigned representative at the number below. Applicants thank the Examiner in advance for this courtesy.

The Director is hereby authorized to charge or credit any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 04-1105, under Order No. 71526-56238.

Respectfully submitted,

Date: October 18, 2006

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